PROTECTION OF HUMAN SUBJECTS IN STUDIES FUNDED BY
U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
(USAMRMC) CONDUCTED OUTSIDE THE UNITED STATES

## POINTS TO CONSIDER

A. Are Human Subjects Involved?

1. Does the proposed research provide a detailed description of the involvement of human subjects? What are the characteristics of the subject population, including the anticipated age range and health status? What is the gender and racial/ethnic composition? Are fetuses, pregnant women, children, prisoners, institutionalized or other vulnerable persons involved?

2. Are data about living, identifiable individuals involved in the form of specimens, records, or other data?

3. What are the potential physical, psychological, social, legal or other risks? What is the likelihood of these risks occurring?

4. Are there alternative treatments?

5. What procedures are there to minimize risks, including confidentiality? What kind of medical or professional interaction is available in the case of adverse effects to subjects? Are there methods to monitor data collected to ensure safety of participants?

6. Are the risks to subjects reasonable in relation to anticipated benefits to subjects and to the knowledge expected to result from the research?

B. Is the Research Exempt? On What Basis?

C. Institutional Review Board (IRB)

1. Is there a domestic institutional review board that will review the research and/or is there a local group that fulfill the criteria and perform the functions of an IRB? If so, where is it located?

2. Who are the members? Can the membership criteria in Sec. 107 of the Common Rule (32 CFR 219.107) be fulfilled?

3. Are there any conflicts of interest? For example, the investigator(s) must not be a member for purposes of his/her research, vote, or be present during IRB proceedings except to present his/her research and to answer questions.

4. Does/will the IRB assess:

-Risks to subjects and how they can be minimized?
-Risk/benefit ratios?
-Equitable selection of subjects?
-Informed consent process, context and documentation?
-Confidentiality?
-Special protections for vulnerable subjects?
-Does/will the board meet as often as needed and at least annually?
-Does/will the board keep minutes and records?
-Does the board have sufficient autonomy and authority to be able to disapprove a protocol or to take action to suspend or terminate a protocol?

D. Reporting

How will the research institution report to the Human Subjects Protection Division (HSPD) (and to the IRB) unanticipated problems involving risks to human subjects, instances of serious noncompliance or suspension or termination of IRB approval?

E. Informed Consent

1. What is the process to inform subjects about the study?

2. Are all required elements of informed consent included in the process? If not, why not?

3. Is there any language that would appear to release the institution and/or investigator(s) from any wrong doing?

4. Will a short form or long form be used?

5. Where will research records and documents be kept?

6. Is there a provision to give each participant a copy of the informed consent document?

F. Documentation/Assurances

Does/will the institution provide accurate documentation addressing the following?

1. A statement of principles governing protection of human subjects in the institution in protecting human subjects?

2. The IRB and its membership?

3. The procedures it will follow to conduct initial and continuing review and report findings and noncompliance, and review changes to the protocol?

4. The name of the responsible official who will act for the institution in protecting human subjects?

G. Additional Considerations - Based on Experience in Implementation:

1. It is important to emphasize that human subjects protections are important during the initial formulation of research. Participants need to be aware that there are requirements for descriptions, analysis, review, and documentation.

2. Situations which result in conflicts of interests on an IRB often arise when institutions assemble an IRB with the investigator(s) as a member. Or, if the IRB is the same group that formulates and endorses the scientific approach for the proposed research, there is an inherent conflict of interest. This type of situation should be discussed during initial conversations with foreign collaborators.

3. Informed consent procedures do allow some flexibility in documentation and information given, but justifications

for flexibility must be carefully outlined.

4. Permission from community and/or tribal leaders may be necessary for the success of the project, but it must not substitute for each individual's informed consent. Waiver of individual consent may be made if conditions in 32 CFR 219.116 are met and approved by the IRB.

**QUESTIONS FOR FOREIGN INSTITUTIONS**
**NARRATIVE FORMAT FOR PROVIDING AN ASSURANCE OR**
**DETERMINING AT LEAST EQUIVALENT PROTECTIONS**

1. Please describe what principles govern your institution that address protecting the rights and welfare of human subjects in research (for example, Declaration of Helsinki, Council of International Organizations of Medical Sciences Proposed Guidelines).

2. Please describe the institutional review board (IRB; group to protect human subjects) in your institution which can act to review this protocol to protect human subjects. The IRB must be able to address the following concerns: minimal risk to participants; risks to participants and the benefits to participants and others; fair selection of participants; special protections for vulnerable participants; informed consent of participants and how this will be documented; monitoring data for safety; confidentiality of data.

3 Please describe the membership of the IRB. Who serves as chair? Who are the members and their educational degrees affiliations: (The IRB should include at least five persons: at least one unaffiliated with the institution; one scientist; one non-scientist; both men and women; someone with expertise about the research and who knows about the community(ies) from which participants will be drawn.) The principal investigator(s) or family members will not be part of the IRB proceeding or vote.

4. Please describe how the IRB will conduct its initial and continuing review and how the IRB will be informed promptly of any changes contemplated in the protocol.

5. Please describe the informed consent process and provide a copy of both the English version and a copy of its foreign translation of the document(s) to be used to inform the participants about the research and seek their consent.

If informed consent is not obtained via a written document, please describe how the consent will be obtained. There must be a witness to the oral presentation to sign the document containing the information presented to the participant.

If informed consent is not sought or all the required

elements are not addressed, please indicate the conditions that the IRB cites that are appropriate to justify waiving consent or specific elements.

6. Please describe how you will maintain the research records (copies of research protocols; minutes; review records; correspondence; IRB members, degrees and affiliations; procedures; statements of new findings to give to participants, etc.).

7. Please describe how the IRB, your institution, and the HSPD will be informed of any serious or continuing noncompliance with human subjects protections or if the IRB has suspended or withdrawn its approval.

8. Please provide the signature of the institutional official responsible for this project and for making sure that human subjects are protected.

## ELEMENTS OF INFORMED CONSENT

In seeking informed consent, the following information should be provided to each subject in the consent form.

1. Title of the study and location (complete address) where the study will be conducted.

2. Name of the principal investigator, and associate(s), if applicable, conducting the study.

3. A statement that the study involves research and a clear explanation of the purpose of the research. In general, the structure of the informed consent should:

a. Be written in language that is easily understood by the subject.

b. Use non-medical language that is easily understood by the subject.

c. Provide a translation of the consent form for subjects enrolled in a study who do not comprehend English. The following statement and information is required on the English language version of the translated consent form:

"I certify that this is an accurate and true translation."
The translator's signature, name, address, phone number and TELEFAX number should be included.

4. Include a statement clearly indicating the expected duration of the subject's participation (the number of hours, days, etc).

5. A description of all **procedures** to be followed and identification of any procedures that are experimental. It must be clearly indicated that these procedures are experimental.

   a. Briefly explain the study design relative to what will be done to the subject (in blind or double-blind studies, subjects must be informed that they may receive either the experimental modality or a placebo). If a placebo is used, its contents should be described.

   b. Specify what is required of the subject (hospital visits, blood donation, etc.). If blood is to be drawn, (including serum pregnancy tests) the amount(s) to be drawn should be

expressed in lay terms.

c. For procedures/pharmaceuticals/devices which are experimental, (if an IND/IDE has been secured from the FDA), the subject should be advised that the IND/IDE is permission for the study to be undertaken and does not indicate FDA approval for the routine use of the drug/device in the method proposed in the protocol. If a drug or device covered under an IND/IDE is involved, it must be clearly indicated in the consent form that it is investigational for the purposes of this research.

d. Although a subject may be familiar with procedures, never assume that he/she comprehends everything.

6. A description of any reasonably foreseeable **risks or discomforts** to the subject. Include risks of pregnancy and possible risks to the fetus, if applicable. It should be clearly indicated if pregnant women will be excluded and/or withdrawn from the study.

a. For studies of potential benefit, describe risks unique to the study; estimate their severity and likelihood; and/or compare these risks with risks which the subject might encounter in the course of his/her daily activities. If similar research has been conducted in the past, describe the incidence of adverse effects or injuries occurring in previous subjects.

b. For studies of no potential benefit to the subject, list all risks which are more than "minimal" (not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine medical tests).

7. A description of any **benefits** to the subject or to others which may reasonably be expected from the research (mention remuneration, if any). If subjects are to be paid for participation in a research study, those payments should not be unduly large. Lump sum payments where all or most of the payment for study participation is withheld until completion of the study should be avoided since this situation may present questions of coercion of subjects to volunteer for, or continue with, a research study.

8. A disclosure of appropriate **alternative procedures** or courses of treatment, if any, that might be advantageous to the subject (e.g., whether treatment is available outside of the protocol).

9. A statement describing the extent, if any, to which **confidentiality** of

records identifying the subject will be maintained. It should be noted that representatives from the U.S. Army Medical Research and Materiel Command (and, where applicable, the Food and Drug Administration and the U.S. Army Medical Department Center and School) may inspect the records of the research.

10. For U.S. Army Medical Research and Materiel Command sponsored research, the following statement **must** be incorporated into the consent form: The United States Department of Defense is funding this research. Should you be injured as a direct result of participating in this research project, you will be provided medical care, at no cost to you, for that injury. You will not receive any injury compensation, only medical care. You should also understand that this is not a waiver or release of your legal rights. You should discuss this issue thoroughly with the principal investigator before you enroll in this study.

11. An explanation of (names and telephone numbers)
    (**a**) whom to contact for answers to pertinent questions **about the research** study and in the event of a research-related **injury** to the subject [should be the investigator];

    (**b**) whom to contact for answers to pertinent questions about research subjects' **rights** [should be the IRB or legal office].

12. A statement that participation is **voluntary**, that refusal to participate will involve **no penalty or loss of benefits** to which the subject is otherwise entitled, and that the subject may **discontinue participation** at any time without penalty or loss of benefits to which the subject is otherwise entitled.

13. Provide **space** for date, signature, typed/printed name and permanent address of subject and signature and typed/printed name of witness.

14. The subject and the witness should be instructed to initial and date all but the last page of the consent form.

15. If the samples donated in this study will be used in other studies, the statement "I understand that there is a possibility that the blood, tissue, body fluid, product, or sample(s) (specify type) which I am providing under this study may also be used in other research studies and could potentially have some commercial applicability." should be included in the consent

form. In addition, **a donation form** must be prepared for signature by the volunteer which states "I voluntarily and freely donate any and all blood, tissues, body fluid, product, or sample(s) (specify type) to the study sponsor (insert institution name) and hereby relinquish all right, title and interest to said items." The title of the study should be inserted at the top of the form. (These samples that will be stored must contain no personal identifiers.)

16. If pregnant women will be excluded, the following statement must be included: "In order to participate in this study, I should have avoided becoming pregnant from the first day of my most recent menses. I should avoid becoming pregnant for at least [time period in days, weeks or months] after [study end date, receipt of drug, etc.]. Pregnancy within [time period in days, weeks or months] after [study end date, receipt of drug, etc.] may create a potential risk to the unborn baby. To avoid becoming pregnant, I should either abstain from sexual relations or practice a method of birth control. Except for surgical removal of the uterus, birth control methods such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm killing products are not totally effective in preventing pregnancy. The only ways to completely avoid risk to the unborn baby are (1) to not become pregnant or (2) do not receive this drug. Adverse effects might affect a developing fetus. Further, might result in unknown risks of deformities or death to the unborn baby. A negative pregnancy test does not absolutely prove that you are not pregnant. regardless of the results of the pregnancy test which you were administered as part of the screening for this study, you should not participate if you think there is a possibility that you might be pregnant." <u>also,</u> a statement should be included which directs the volunteer to notify the principal investigator if she becomes pregnant. If women will be withdrawn from the study if they become pregnant, that should be clearly indicated.

17. Any additional costs to the subject must be clearly indicated.

18. For all studies involving more than minimal risk, the following statement must be included in the consent form: "It is the policy of the U.S. Army Medical Research and Materiel Command (USAMRMC) that data sheets are to be completed on all

volunteers participating in research for entry into the USAMRMC's Volunteer Registry Data Base. The information to be entered into this confidential data base includes your name, address, social security number, study name and dates. The intent of the data base is two fold: first, to readily answer questions concerning an individual's participation in research sponsored by USAMRMC; and second, to ensure that the USAMRMC can exercise its obligation to ensure research volunteers are adequately warned (duty to warn) of risks and to provide new information as it becomes available. The information will be stored at USAMRMC for a minimum of 75 years. "

(Revised June 1998)

(Type on Institution Letterhead)

ASSURANCE OF PROTECTION FOR HUMAN SUBJECTS IN INTERNATIONAL RESEARCH SPONSORED BY THE U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND

_____(Name of Institution)_____, hereinafter known as the "institution", hereby gives assurance that it will comply with the principles and procedures for protecting human research subjects specified below.

## PART I

## ETHICAL PRINCIPLES AND INSTITUTIONAL POLICIES GOVERNING RESEARCH INVOLVING HUMAN SUBJECTS

### I. Ethical Principles Governing Human Subjects Research

This institution is guided by the ethical principles regarding research involving human subjects set forth in the _____. These ethical principles guide the institution in the conduct of all its human subjects research.

Note: In Section I above, the institution may choose to cite the Belmont Report, the Declaration of Helsinki, or other appropriate code, declaration, or statement of principles that is consistent with the terms of this Assurance.

### II. Institutional Policies Governing Human Subjects Research

A. This institution acknowledges and accepts its responsibilities for protecting the rights and welfare of all human subjects involved in the research which it sponsors or conducts.

B. This institution encourages and promotes an

institutional atmosphere that safeguards the rights and welfare of human subjects.

C. It is the policy of this Institution that before human subjects are involved in research which it sponsors or conducts, proper consideration must be given to:

(1) the risks to the subjects,
(2) the anticipated benefits to the subjects and others,
(3) the importance of the knowledge that may reasonably be expected to result, and
(4) the informed consent process to be employed.

D. Whenever appropriate, it is the policy of this institution to consider special safeguards for protecting research subjects who may be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

## PART 2

## HUMAN SUBJECT PROTECTIONS FOR RESEARCH FUNDED BY THE U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND

### I. Applicability

Part 2 of this Assurance applies only to the following research project which is conducted or sponsored by this institution and supported by the DOD:

Project Title:_____

Project/Contract Number:_____

Project Investigator/Director:_____

## II. Institutional Responsibilities

A. This institution recognizes that all human subjects research supported by the U.S. Army Medical Research and Materiel Command, including the project referenced above, must be conducted in accordance with the United States Federal Policy for the Protection of Human Research Subjects.

B. The Institutional Review Board (IRB) listed in Attachment A has been designated to be responsible for the initial and continuing review of the project referenced above. The IRB includes at least five persons, including at least one scientist, one non-scientist, and one person not otherwise affiliated with the institution. Every nondiscriminatory effort has been made to include both women and men. The IRB also includes persons who are sensitive to the concerns of the population from which subjects will be recruited.

C. Provisions have been made to provide both meeting space for the IRB and sufficient staff to support the IRB's review and record keeping duties.

D. The institution will fully comply with Title 10, United States Code, Section 980 which states: if an individual cannot give his/her own consent, and there is no intent to benefit the subject (for example, minors) he/she cannot be entered into a study funded by the DOD. <u>This is legally binding and there will be no exceptions.</u>

## III. IRB Responsibilities

A. The project referenced above has been and will be reviewed at convened meetings at which a majority of IRB members are present. A majority vote of those members present at the meeting is required for approval. The research investigators and their family members may not participate in IRB proceedings except to provide information requested by the IRB.

B. The IRB used the following criteria to determine that protections for human research subjects in this project are adequate:

(1) Risks to subjects are minimized.
(2) Risks to subjects are reasonable in relation to

anticipated benefits.

(3) Selection of subjects is equitable.

(4) When appropriate, the data collected will be monitored during the course of the study to ensure safety of subjects.

(5) Privacy of subjects and confidentiality of data are protected.

C. The IRB has determined that legally effective informed consent will be obtained under circumstances that provide sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. Copies of all informed consent documents for this project will be provided.

D. The IRB will review, and have the authority to approve, require modification in, or disapprove project changes.

E. Continuing reviews by the IRB will be conducted at intervals appropriate to the degree of risk, but not less than once per year. Copies will be provided to the Human Subjects Protection Division (HSPD). The IRB may be called into an interim review session by the Chairperson at the request of any IRB member or Institutional Official to consider any matter concerned with the rights and welfare of any subject.

F. The IRB will maintain documentation of its activities to include copies of research protocols, minutes of IRB meetings and continuing review records, correspondence with investigators, IRB membership with degrees and affiliations, IRB operating procedures, and statements of new findings provided to subjects. This documentation will be retained for at least three years after the completion of the project and will be accessible for inspection and copying by representatives of the United States Government.

G. The IRB will report promptly to appropriate institutional officials and to the HSPD:

(1) Any unanticipated problems or injuries involving risk to subjects or others.

(2) Any serious or continuing noncompliance with this Assurance or with the requirements or determinations of the IRB.

(3) Any changes in this project which are reviewed

and approved by the IRB.

(4) Any suspension or termination of IRB approval.

## IV. Responsibilities of Project Investigators/Directors

A. Project investigators/directors accept their responsibility to comply with the stipulations of the IRB and with the terms of this Assurance.

B. Project investigators/directors will report promptly to the IRB proposed changes in this project, and changes will not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the subjects.

C. Project investigators/directors will report promptly to the IRB any unanticipated problems or injuries involving risks to subjects or others.

## V. Institutional Review Board (IRB) Membership

Name of IRB Agency_____
_____

Address, Phone No. and TELEFAX of Chairperson_____
_____
_____
_____

| Members' Names | | | Highest Degree | Scientific Specialty | Affiliation With Institution |
|---|---|---|---|---|---|
| First | MI | Last | Earned | | |
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**PART 3**
**INSTITUTIONAL ENDORSEMENT AND CERTIFICATION**

Project Title:_____

Project Number:_____

Project Investigator/Director:_____

Date of IRB Approval:_____

The officials signing below assure that the project referenced above was approved by the IRB on the date indicated and that the project will be conducted in accordance with all provision of this Assurance and of the United States Federal Policy for the Protection of Human Research Subjects.

**I. Authorized Official of the Institution Providing This Assurance**

Signature_____Date:_____

Name:_____TELEFAX:_____

Title:_____Telephone:_____

Complete Address:_____

**II. Authorized Official of the Institution With the IRB (Required <u>only</u> if <u>different</u> from the institution listed above)**

Signature:_____Date:_____

Name:_____TELEFAX:_____

Title:_____Telephone:_____

Complete
Address:_____

**III. IRB Chairperson**

Signature:_____

Date:_____TELEFAX:_____

Title:_____Telephone:_____

Complete
Address:_____

**PART 4**
**FEDERAL COMPONENT AGENCY APPROVAL**

Project
Title:_____

Project
Number:_____

Project
Investigator/Director:_____

Date of IRB
Approval:_____
This is to certify that all parts of this Assurance are in compliance with the requirements of the Federal Policy for the Protection of Human Research Subjects.

Federal Component Agency Approving Official:

Signature:_____Date:_____

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Assurance Number _____